In the Office Action dated September 14, 2001, claims 1, 7-9 and 11 were rejected under 35 U.S.C. § 103(a) as unpatentable over Chatta et al. (Proc. Am. Assoc. Cancer Res. 38:403, abstract #2703, March 1997). This rejection is respectfully traversed.

The present application claims priority to provisional application 60/048,406 which was filed June 3, 1997. The abstract of Chatta et al. appeared in a March 1997 issue, and was thus published less than one year prior to the filing date of Applicants' provisional application. To expedite prosecution, a Declaration (pursuant to 37 C.F.R. § 1.131) will be forthcoming to antedate the Chatta et al. abstract.

Therefore, it is believed that, upon filing of the Rule 131 Declaration, this rejection of claims 1, 7-9 and 11 under 35 U.S.C. § 103(a) will have been overcome. Withdrawal of this rejection upon filing of the Declaration is respectfully requested.

In the Office Action, claims 1, 7, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Disis et al. (J. Immunol. 156:3151-3158, May 1996) in view of any one of Dyrberg et al. (Current Topic in Microbiology and Immunology 130:25-37, 1986), or Naftzger et al. (Proc. Natl. Acad. Sci. USA 93:14809-14814, Dec. 1996), or Mamula (Arthritis and Rheumatism, Vol. 35, suppl., p.S38, 1992), or Fedoseyeva et al. (Transplantation 61:679-683, 1996), or Mahi-Brown et al. (J. Reproductive Immunology 21:29-46, 1992). This rejection is respectfully traversed.

As described above, a Rule 131 Declaration will be forthcoming to antedate the abstract of Chatta et al. from March 1997. The Declaration will also antedate Naftzger et al. which was published December 1996 and thus was published less than one year prior to the filing date of Applicants' provisional application. Accordingly, upon filing of the Declaration, Naftzger et al. is no longer available as a citable reference and cannot be used alone or in combination with another reference to reject the pending claims.

It is respectfully submitted that there was no support within the meaning of Section 103(a) to permissibly combine Disis et al. with another reference in an attempt to establish obviousness. At the time of the subject invention, there was no teaching or suggestion to combine the teachings of the prior art as attempted by the Office Action. Absent a teaching or suggestion that the combination be made, obviousness cannot be established by such a combination. Disis et al. disclosed that intact rat HER-2/neu protein failed to elicit rat

neu-specific immunity in rats. However, rather than attempt to manipulate the conditions of immunization with whole protein, Disis et al. chose to evaluate immunization to peptides (Disis et al. at page 3157, left column, first paragraph). Disis et al. successfully elicited rat neu-specific immunity in rats by immunizing with rat HER-2/neu peptides. Their use of peptides circumvented the tolerance to self protein observed when intact protein was used. As stated in the abstract (page 3151) of Disis et al.: "These studies suggest an immunization strategy" [the use of human HER-2/neu peptides to immunize humans] "that might be effective in human cancer vaccines targeting self tumor Ag." Therefore, due to the success in Disis et al. of overcoming self tolerance (by the use of peptides from the same species as immunized), not only does Disis et al. not teach or suggest the combinations of references attempted in the Office Action, but Disis et al. actually teaches away from the immunization strategy of the present invention and thus away from combining references to attempt to reconstruct the strategy of Applicants.

Even assuming for the sake of argument that it would be permissible to combine Disis et al. with one of the other cited references, it is respectfully submitted that such combinations fail to establish a *prima facie* case for obviousness. (It is noted that, as discussed above, Naftzger et al. is being removed as citable prior art by way of Declaration. Therefore, there cannot be a combination of Disis et al. and Naftzger et al., and as such it is not discussed herein.) In the Office Action, Disis et al. is combined with any one of Dyrberg et al.; Mamula; Fedoseyeva et al.; or Mahi-Brown et al. Each of these combinations is addressed in turn.

Disis et al. and Dyrberg et al. is one combination of references for this rejection under § 103(a). Dyrberg et al. focuses on the initiation of autoimmune responses by foreign pathogens, particularly induction by viruses. Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) is directed to a method involving human self tumor antigens. Dyrberg et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the molecular mimicry of Dyrberg et al. to the human self tumor antigen (HER-2/neu) of Disis et al. Another combination is Disis et al. and Mamula for this rejection under § 103(a). The pending claims are directed to methods including human self tumor antigens. Mamula discloses the use of cytochrome c to initiate autoimmune responses. Mamula provides no teaching

regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the cytochrome c autoimmunity of Mamula to the human self tumor antigen (HER-2/neu) of Disis et al. Another combination is Disis et al. and Fedoseyeva et al. for this rejection under § 103(a). The pending claims are directed to methods involving human self tumor antigens. Fedoseyeva et al. focuses on elucidating the immune mechanisms underlying long term allograft rejection following transplantation. Fedoseyeva et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the transplantation teachings of Fedoseyeva et al. to the human self tumor antigen (HER-2/neu) of Disis et al. The final combination is Disis et al. and Mahi-Brown et al. for this rejection under § 103(a). The pending claims are directed to methods involving human self tumor antigens. Mahi-Brown et al. discloses the cellular immune response to immunization with zona pellucida antigens. Mahi-Brown et al. provides no teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the zona pellucida teachings of Mahi-Brown et al. to the human self tumor antigen (HER-2/neu) of Disis et al.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of the pending claims.

Therefore, it is believed that this rejection of claims 1, 7, 11 and 12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7-9, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Spitler et al. (U.S. Patent No. 5,925,362) in view of any of Dyrberg and Oldstone, or Naftzger et al., or Mamula, or Fedoseyeva et al., or Mahi-Brown et al. This rejection is respectfully traversed.

It is respectfully submitted that there was no support within the meaning of Section 103(a) to permissibly combine Spitler et al. with another reference in an attempt to establish obviousness. At the time of the subject invention, there was no teaching or suggestion to combine the teachings of the prior art as attempted by the Office Action. Absent a teaching or suggestion that the combination be made, obviousness cannot be established by such a combination.

Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) recites in part "with an amino acid sequence native to a non-human source." Spitler et al. does not teach or suggest immunizing with an amino acid sequence native to a non-human source. Therefore, Spitler et al. taken alone does not establish a *prima facie* case for obviousness.

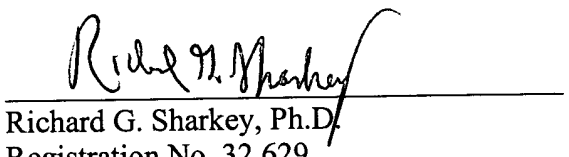
As discussed above, there is no basis in the cited art for combining Spitler et al. with any of the other cited references. Even assuming, for the sake of argument, that it would be permissible to combine Spitler et al. with one of the other cited references, it is respectfully submitted that such combinations fail to establish a *prima facie* case for obviousness. (It is noted that, as discussed above, Naftzger et al. is being removed as citable prior art by way of Declaration. Therefore, there cannot be a combination of Spitler et al. and Naftzger et al., and as such it is not discussed herein.) Claim 1 (and therefore claims 7-9 and 11-12 which depend therefrom) is directed to a method involving human self tumor antigens. As described above, none of Dyrberg et al., Mamula, Fedoseyeva et al., or Mahi-Brown et al. provide any teaching regarding tumor related proteins. At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the non-tumor related teachings (of Dyrberg et al., Mamula, Fedoseyeva et al., or Mahi-Brown et al.) to the human self tumor antigens of Spitler et al.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of the pending claims.

Therefore, it is believed that this rejection of claims 1, 7-9, 11 and 12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

Therefore, in light of the remarks set forth above, Applicants believe all the Examiner's rejections have been overcome, pending filing of the Rule 131 Declaration. Reconsideration of the application and allowance of all pending claims (1,7-9 and 11-12) are respectfully requested. If there is any further matter requiring attention prior to allowance of the subject application, the Examiner is respectfully requested to contact the undersigned attorney (at 206-622-4900) to resolve the matter.

Respectfully submitted,
Seed Intellectual Property Law Group PLLC



Richard G. Sharkey, Ph.D.
Registration No. 32,629

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